

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Patent Application of:

David C. Baulcombe et al.

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For: RNA MOLECULES AND VECTORS FOR  
GENE SILENCING

Confirmation No. 4500

Art Unit: 1635

Examiner: Amy Bowman, Ph.D.

DECLARATION OF DAVID CHARLES BAULCOMBE  
UNDER 37 C.F.R. § 1.132

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

I, David Charles Baulcombe, declare as follows:

1. I am a co-inventor in the above-referenced case. I hold the position of Senior Scientist at the Sainsbury Laboratory. I am a Fellow of the Royal Society, the UK's National Academy of Science and a Foreign Associate Member of the US National Academy of Sciences. From September 2007 I will be Professor of Botany and Royal Society Research Professor at the University of Cambridge. I have practiced in the field of gene expression and related technology since at least 1978. A copy of my *curriculum vitae* is attached hereto as Exhibit A.

2. On page 24 of our above-referenced application at lines 6-29, we describe an experiment in which an approximately 25-nucleotide glucuronidase (GUS) antisense RNA was detected in two of three tobacco cell lines that carry a transgene for this protein. Neither the 25-nucleotide GUS RNA nor PTGS was detected in the third cell line, which contained a transgene

suppressor of the promoter associated with the GUS encoding sequence. Thus, the GUS encoding sequence in this third tobacco line could not be transcribed.

3. On page 27 of the application, we state that the dependence of the 25-nucleotide GUS antisense RNA accumulation on sense transcription of a GUS transgene supports an RNA template model, but it would be not possible to distinguish from these results whether the antisense RNA is made directly as a 25-nucleotide species or as longer molecules that are subsequently processed. However, in either case, because the sense strand of the GUS RNA must be used as a template for the production of the antisense RNA's detected, the sense and antisense RNA's involved in PTGS must necessarily be substantially complementary.

4. I therefore believe the only way to interpret the results of the experiment set forth on page 24, which demonstrates that the presence of sense RNA is needed in order for the small antisense RNA molecules to be obtained, is that they demonstrate that the small antisense RNA must be complementary to a sense strand.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Executed at NORWICH, NORFOLK, UK, on 23 May 2007.  
(city) (state) (country) (day) (month)

David Baulcombe  
2 DAVID BAULCOMBE

(David Charles Baulcombe)

# David Baulcombe – contact details and cv

## Contact details until September 2007

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after September 2007 I will be at The Department of Plant Sciences in Cambridge University

## Personal

D.O.B: 7 April 1952, Solihull, Warwickshire, UK; British citizen; married with four children; interests include music, sailing and hill walking

## Degrees

1970 - 1973	University of Leeds B.Sc (I) - Botany
1973 - 1977	University of Edinburgh Ph.D - Botany

## Career

Jan. 1977-Nov. 1978 McGill University, Montreal, Canada  
Post-doctoral Fellow  
Dec. 1978-Dec. 1980 University of Georgia, Athens, GA  
Post-doctoral Fellow  
Dec. 1980-Aug.1988 Plant Breeding Institute, Cambridge, UK  
Higher Scientific Officer (from April 1986 Principal Scientific Officer)  
Aug.1988- September 2007 The Sainsbury Laboratory, Norwich, UK  
Senior Research Scientist and Head of Laboratory (from 1990-1993 and 1999-2003), Professor of University of East Anglia (2002-)  
September 2007 onwards – Professor of Botany and Royal Society Research Professor, University of Cambridge, Cambridge UK

## Honours and Awards

Royal Medal (2006) The Royal Society; Massry Prize (2005) Massry Foundation - University of Southern California (shared with Fire and Mello); Foreign Associate Member of the National Academy of Sciences (USA) (elected 2005); M.W. Beijerinck Virology Prize (2004) Royal Netherlands Academy of Arts and Sciences Wiley Prize in Biomedical Science (2003) (Wiley Foundation - Rockefeller University - shared with Fire, Mello and Tuschl); Academia Europaea, Member (elected 2002); Ruth Allen Award, American Phytopathology Society (2002); Kumho Science International Award in Plant Molecular Biology and Biotechnology (2002) Kumho Cultural Foundation, Korea; Fellow of the Royal Society (elected 2001); President International Society of Plant Molecular Biology (2003-2004); Honorary Professor, University of East Anglia (1998-2002); European Molecular Biology Organisation, Member (elected 1997); Prix des Cerealiers de France (1990) for work on hormonally regulated genes of cereals

## Miscellaneous

Editorial: The Plant Journal (1991-); Virology (1996-); EMBO Journal (1999- ; Senior Advisor 2005- ) and EMBO Reports(Editorial Board) (1999-); Genome Biology (2005-); Cell Host and Microbe (2007-) **Scientific Advisory Board**, National Institute for Biological Sciences, Beijing (2006-2009); National Institute of Chemical Physics and Biophysics, Tallinn, Estonia. Science Foundation Ireland (2004-7) **Panel member**, HSE Scientific Advisory Committee on Genetic Modification (Contained Use)(2004-2007)

## Current grant funding

2231 BBSRC Ref. BB/C006739/1 - 'Arabidopsis agonaute ribonucleoproteins in RNA silencing' start 14-6-2005 - 13-7-2008 £286K.

2242 BBSRC Ref BB/E004091/1 'A computational platform for the high-throughput identification of short RNAs and their targets in plants' start 1-2-2007 - 31-1-2010. £84K

2243 BBSRC BB/E006981 'SIROtyping: siRNA and miRNA profiles of tomato' start 1-3-2007-31-12-2009 £684K

2244 EUFP6 - EU Integrated grant 'SIROCCO' start 1-1-2007 - 31-12-2011 E11.7M

2223 EU HPRN-CT-2002-00257 EU training network - 'Silencing in Different Organisms' start 1-12-2002 - 30-11-2006 £152K

2227 BBSRC 83/P18617 'The molecular mechanism of activation of NBS-LRR proteins' start 1-1-2003 - 5-9-2006 £263K

2234 DuPont grant 'Gene Silencing Techniques' start 1-10-2005 - 30-9-2006 £61K

## Publications

Results found: 164

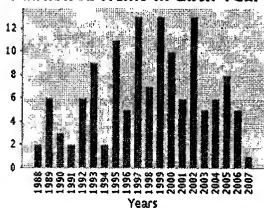
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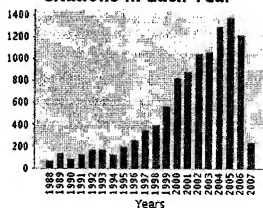
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**Baulcombe, D. (2007a).** Amplified Silencing. *Science* **315**, 199-200.

**Baulcombe, D. (2007b).** Short Silencing RNA: The Dark Matter of Genetics? Cold Spring Harbor Laboratory Press, New York **LXXI** in press.

**Baurle, I., Smith, L.M.A., Baulcombe, D., and Dean, C. (2007).** Widespread role for the flowering time regulators FCA and PPA in siRNA-directed chromatin silencing. to be submitted.

**Hernandez-Pinzon, I., Yelina, N.E., Schwach, F., Studholme, D.J., Baulcombe, D., and Dalmay, T. (2007).** SDE5, the putative homologue of a human mRNA export factor, is required for transgene silencing and accumulation of *trans*-acting endogenous siRNA. *The Plant Journal* **50**, 140-148.

**Molnar, A., Schwach, F., Studholme, D.J., Thuenemann, E., and Baulcombe, D. (2007).** miRNAs control gene expression in single cell alga *Chlamydomonas reinhardtii*. *Nature* in press

**Smith, L.M., Pontes, O., Searle, I., Yelina, N.E., Yousafzai, F.K., Herr, A.J., Pikaard, C., and Baulcombe, D. (2007).** A novel SNF2 protein associated with nuclear RNA silencing and spread of a silencing signal between cells in Arabidopsis. *The Plant Cell* in press

- Tameling, W.L.L., and Baulcombe, D.** (2007). Physical association of the NB-LRR resistance protein Rx with a Ran GTPase activating protein is required for extreme resistance to potato virus X. *Plant Cell in press*
- Farnham, G., and Baulcombe, D.** (2006). Artificial evolution extends the spectrum of viruses that are targeted by a disease-resistance gene from potato. *Proceedings Of The National Academy Of Sciences Of The United States Of America* **103**, 18828-18833.
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